Environmental Research Section A **85,** 256–259 (2001)
doi:10.1006/enrs.2000.4224, available online at http://www.idealibrary.com on IDEAL®

Pesticide Use by Persons Who Reported a High Pesticide Exposure Event in the Agricultural Health Study[1]

Sarah A. Keim and Michael C. R. Alavanja

Occupational Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892

Received April 26, 2000; published online January 23, 2001

Almost 16% of the pesticide applicators in the Agricultural Health Study (AHS) cohort (a cohort that includes 52,629 private applicators) reported having a high pesticide exposure event (i.e., an incident or experience while using a pesticide that caused an unusually high personal exposure). Pesticides involved in these events were compared to the frequency with which specific pesticides were ever used by the AHS cohort. Generally, pesticides with greater acute toxicity were more frequently involved with the high pesticide exposure event than were other pesticides. Whereas it is clear that the use of acutely toxic pesticides may be related to more frequent visits to health care facilities, the reason that the spills and immersions of the high pesticide exposure events are associated with the acute toxicity of the pesticide is not intuitively clear. This analysis suggests that current practices directed at minimizing pesticide exposures may not be sufficient for acutely toxic or irritating chemicals.

Key Words: **pesticides; pesticide poisoning; accidental exposures; farmers; noncancer toxicity.**

INTRODUCTION

Both acute and chronic exposures to pesticides can produce adverse health outcomes (Baker *et al.*, 1990). High pesticide exposure events (HPEEs), resulting from spills and other accidents, can involve high acute pesticide exposures (Ogilvie *et al.*, 1990; Kross *et al.*, 1992). Until recently, few studies have examined the circumstances surrounding these events. An initial report from the Agricultural Health Study characterized the work practices of individuals who reported HPEEs. Work practices such as delaying changing clothing or washing, washing clothing with the family laundry, washing inside the house, applying pesticides within 50 yards of a well, and storing pesticides in the home were significantly more frequent in those who reported a HPEE than in those who did not. First pesticide use more than 10 years ago and self-repair of equipment were also more common among those reporting a HPEE (Alavanja *et al.*, 1999). As expected, the probability of a HPEE increases as the number of pesticide applications increases (Alavanja *et al.*, 1999; Mage *et al.*, 2000). Almost 16% of the pesticide applicators in the study cohort reported having "an incident or experience while using any pesticide which caused an unusually high personal exposure." This study expands upon previous analyses by examining the pesticides involved in HPEEs and comparing them to pesticides routinely used by the pesticide applicators.

The primary focus of the Agricultural Health Study is the evaluation of cancer and other disease outcomes resulting from agricultural exposures, including pesticide exposures. Studying HPEEs is an essential component of a comprehensive lifetime exposure assessment for pesticides in an epidemiologic study since high-exposure incidents make up an important, documentable part of overall exposure (Ogilvie *et al.*, 1990; Kross *et al.*, 1992).

MATERIALS AND METHODS

Methods used in the Agricultural Health Study have been previously described (Alavanja *et al.*, 1996). Pesticide applicators enrolled in a private or commercial applicator licensing course in Iowa or North Carolina or taking a licensing exam in Iowa were invited to participate, as were the spouses of

[1]This work was supported by Contracts N01-CP-33047, N01-CP-33048, and N01-CP-21095 and was conducted in accordance with national and institutional guidelines for the protection of human subjects.

0013-9351/01 $35.00

the private applicators in Iowa and North Carolina. A total of 52,629 private applicators completed an enrollment questionnaire, and 22,884 (43.5%) completed a supplemental mail-in questionnaire. Questions concerning high pesticide exposure events are contained in the supplemental mail-in questionnaire. Questions about pesticide exposure are contained in both the enrollment and the supplemental questionnaire. This study is based on data from both questionnaires and involves a subset of the total participants ($n = 3635$ cases and 14,542 controls). A previous study has shown that the respondents who completed the supplemental mail-in questionnaire were older and had smaller farms than those who completed only the enrollment questionnaire, but the differences were small and should not bias generalizations to the total cohort (Tarone *et al.*, 1997).

Cases were the 3635 respondents (15.88%) who answered "yes" to "Have you ever had an incident or experience while using any type of pesticide which caused you unusually high personal exposure?" Controls (14,542 applicators) were selected from the respondents who reported "no" to this question. The control group served as an internal comparison group that allowed us to determine whether there were any inherent differences between the specific chemicals used routinely by cases and controls that made cases more likely to have a HPEE. Cases and controls were matched on age, state, and gender. The cases included 1 woman in the 76 to 80 years age range that had only 2 controls to match on these variables.

Respondents were asked about use of 50 major pesticides in the enrollment questionnaire. The supplemental questionnaire asked about ever/never use of an additional 80 pesticides. Responses to the questions about ever/never use were illegible for a few respondents; so, we treated those responses as missing.

Respondents were asked "What was the name of the product you were using during your highest exposure incident or experience?" More than one pesticide could be listed; so, involvement in HPEEs by all of the pesticides combined totals greater than 100%. Our analysis focused on 36 pesticides, the pesticides involved in 1% or more of all HPEEs (Alavanja *et al.*, 1999). of the 3635 cases, 258 (7.1%) had missing data, and 731 (20.1%) listed an "other" pesticide (i.e., a pesticide other than the 36 selected pesticides). The responses from the remaining 2646 cases (72.8%) were coded as one of the 36 pesticides of interest. One respondent described a HPEE that was clearly related only to military service and was excluded from the analysis. Three applicators gave responses such as "a variety of pesticides" and were coded as "other."

We undertook a chemical-specific (e.g., alachlor, atrazine) analysis using the Spearman rank order correlation comparison. First, we compared the proportion of cases ever using a particular pesticide versus controls using that chemical. This analysis would reveal chemical differences in use that may make cases more likely to have a HPEE. Second, we compared the pesticides involved in the high-exposure event to the pesticides ever used by the cases. This comparison helps identify chemicals that are disproportionately involved in HPEEs.

RESULTS

Our first comparisons demonstrated that controls and cases differ very little on what pesticides they ever use. Herbicides are the most commonly used pesticides for cases and controls. Most respondents have used all four classes of chemicals (herbicides, insecticides, fungicides, and fumigants) at some time. The χ^2 goodness-of-fit calculations for the pesticide categories confirmed the similarity between the cases and the controls on routine pesticide use (see Table 1). There was, however, a significant difference between the frequency that cases reported "ever" using a specific pesticide and the frequency that those pesticides were involved in the HPEEs ($P < 0.001$) (i.e., specific pesticides were disproportionately associated with HPEEs).

The pesticide-specific analysis using the Spearman rank order correlation expanded upon these results. The proportion of cases and controls using specific pesticides is very highly correlated ($r = 0.99$) (see Table 1). Meanwhile, when we compared ever/never use of a pesticide to the HPEE pesticides, the correlation is lower ($r = 0.72$) and the rank order is significantly different.

The rank orderings for the HPEE pesticides and the ever/never pesticides for the cases is shown in Table 2. The ever/never rank orderings are the same for the controls. The top 5 HPEE pesticides are alachlor (11.2% of cases reporting a HPEE with this pesticide), 2,4-D (9.9%), trifluralin (9.9%), atrazine (9.3%), and phorate (4.1%); four are herbicides, and phorate is an insecticide. Combined, they are involved in 45% of HPEEs. Alachlor alone is involved in approximately 11% of HPEEs, whereas its use ever/never gives it a rank of 6th. Phorate ranks 5th on the list of HPEE pesticides; yet, its routine use is only 16th. Butylate also appears high on the HPEE list but 15th in the ever/never rank order. Also,

TABLE 1
Pesticides Used by Case vs Control Status

	Comparison by pesticide category[a] (χ^2)
Pesticide ever used by case vs control	2.753 ($P = 0.60$)
Pesticide ever used by case vs pesticide used by case during HPEE	2.324 ($P < 0.001$)
	Comparison by specific pesticide (Spearman coefficient r)
Pesticide ever used by case vs control	0.99
Pesticide ever used by case vs pesticide used by case during HPEE	0.72

[a]Pesticide category refers to the four chemical classes: herbicides, insecticides, fungicides, and fumigants.

pendimethalin is ranked 9th on the HPEE list but 13th in the ever/never rank order. Glyphosate is very commonly used by applicators, yet is involved in only 2.3% of HPEEs and ranks 11th. Sixty-seven percent of applicators reported using dicamba but its involvement in HPEEs is less common, ranking 14th on the HPEE list. Finally, imazethapyr ranks 10th ever/never and 28th on the HPEE ranking, involved in only 0.8% of HPEEs. The pesticides 2,4-D, trifluralin, atrazine, metolachlor, malathion, and cyanazine appear on both rank orderings at nearly the same positions.

TABLE 2
Rank Order of Top 10 Pesticides Most Commonly Used by Respondents Reporting a HPEE (Percentage Reporting Use)

HPEE pesticides	Ever/never pesticides used by cases*
Alachlor (11.2%)	2,4-D (88.4%)
2,4-D (9.9%)	Glyphosate (85.8%)†
Trifluralin (9.9%)	Atrazine (82.0%)
Atrazine (9.3%)	Malathion (77.5%)
Phorate (4.1%)†	Trifluralin (67.4%)
Metolachlor (4.1%)	Dicamba (67.2%)†
Butylate (3.1%)†	Alachlor (65.7%)
Malathion (2.8%)	Metolachlor (60.2%)
Pendimethalin (2.7%)†	Cyanazine (57.3%)
Cyanazine (2.5%)	Imazethapyr (55.2%)†

*Same as the rank order for ever/never pesticides used by controls.

†Pesticides not linked by an arrow rank lower than 10th in the opposite rank order.

DISCUSSION

Pesticide toxicity, in addition to work practices (Alavanja *et al.*, 1999), appears to be a contributing factor to HPEE occurrence. For example, cases and controls have used roughly the same pesticides historically, signifying that no significant differences exist in the pesticides used by cases and controls that would make cases more likely to have a HPEE than controls. Yet, several pesticides appearing high on the HPEE pesticides rank order list are much lower on the ever/never rank order list. Alachlor accounts for a disproportionate percentage of HPEEs. Many people are very sensitive to alachlor products and experience allergic symptoms (R. Hartzler, personal communication). These effects, in addition to its historically high use, may explain alachlor's position at the top of the list. Phorate is a highly toxic compound that is highly irritating to the skin and eyes (Pesticide Fact Handbook, 1988) and ranks 5th on the HPEE rank order list but only 16th on the ever/never rank order list. Butylate is a strong eye irritant, as evidenced by its designation in EPA Toxicity Category I for eye irritation (R.E.D. Facts, Butylate, 1993) and is 7th on the HPEE rank order list but only 15th on the ever/never list. Meanwhile, some frequently used pesticides are rarely involved in HPEEs, for example, glyphosate and imazethapyr, which are much less toxic to the skin and eyes than alachlor and butylate (Pesticide Fact Handbook, 1988). One exception is dicamba, a chemical that is highly irritating to the eyes. It appears high on the ever/never list but lower on the HPEE list. Like many of the chemicals high on the ever/never list, its overall toxicity is relatively low. One might expect it to be involved in a greater percentage of HPEEs than is demonstrated by these data. Pendimethalin has a similar rank on both lists, 9th on the HPEE list and 13th on the ever/never list.

The toxicity of a pesticide should not necessarily be directly related to its frequency of involvement in unusually high pesticide exposure events (i.e., HPEE) if proper safety precautions are used. Two scenarios may explain why certain pesticides are frequently involved in HPEEs. First, if an applicator experiences symptoms or illness or visits a health care provider (which are more likely to result from a HPEE with a toxic chemical), he or she is more likely to remember the event. Second, pesticides that are neurotoxins, eye irritants, and/or allergens may produce an impairment in physical or mental dexterity that could increase the probability of having a HPEE with that chemical.

Our analysis shows that the pesticides involved in HPEEs differ from those ever used by applicators in this cohort. We have provided possible explanations for the occurrence of HPEEs in this cohort, but further study is needed to establish the reasons that some chemicals are disproportionately associated with high-exposure events. Understanding the circumstances of HPEEs can help prevent such poisonings and reduce lifetime exposure.

REFERENCES

Alavanja, M. C. R., Sandler, D. P., McMaster, S. B., Zahm, S. H., McDonnell, C. J., Lynch, C. F., Pennybacker, M., Rothman, N., Dosemeci, M., Bond, A. E., and Blair, A. (1996). The agricultural health study. *Environ. Health Perspect.* **104,** 362–369.

Alavanja, M. C. R., Sandler, D. P., McDonnell, C. J., Mage, D. T., Kross, B. C., Rowland, A. S., and Blair, A. (1999). Characteristics of persons who self-reported a high pesticide exposure event in the agricultural health study. *Environ. Res.* **80,** 180–186.

Baker, S. R., and Wilkinson, C. F. (1990). "The Effects of Pesticides on Human Health," Advances in Modern Environmental Toxicology, Vol. 18. (M. A. Mehlman, Series Ed.) Princeton Sci. Pub., Princeton, NJ.

Hartzler, R. Assistant Professor of Agronomy and Extension Weed Specialist, Iowa State University and Iowa State University Extension Service. Personal communication.

Kross, B. C., Slim, M. I., Hallberg, G. R., Bruner, D. R., and Cherryholmes, K. (1992). Pesticide contamination of private well water, a growing rural health concern. *Environ. Int.* **18,** 231–241.

Mage, D. T., Alavanja, M. C. R., Sandler, D., McDonnell, C. J., Kross, B., Rowland, A., and Blair, A. (2000). A model for predicting the frequency of high pesticide exposure events in the agricultural health study. *Environ. Res.*, in press.

Ogilvie, L. K., Kross, B. C., Popendrof, W. J., Burmeister, L. F., Fuortes, L., and Ballas, Z. (1990). Summary report: Assessment methods for pesticide exposure (AMPE) study. *In* "NCI Progress Report, Institute of Agriculture Medicine and Occupational Health," p. 50. Univ. of Iowa Press, Iowa City.

Pesticide Fact Handbook, Vols. 1 and 2. (1988). U.S. Environmental Protection Agency, Noyes Data Corp., Park Ridge, NJ.

R. E. D. Facts, Butylate. (1993). U. S. Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances. EPA-738-F-93-014.

Tarone, R. E., Alavanja, M. C. R., Zahm, S. H., Lubin, J. H., Sandler, D. P., McMaster, S. B., Rothman, N., and Blair, A. (1997). The agricultural health study: Factors affecting completion and return of self-administered questionnaires in a large prospective cohort study of pesticide applicators. *Am. J. Ind. Med.* **31,** 233–242.